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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/765,491
Filing Date: January 18, 2001
Appellant(s): ARBISER, JACK L.

Patrea L. Pabst
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 1, 2006 appealing from the Office action mailed October 28, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct.

The changes are as follows:

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner.

Claims 4-6 and 17-19 under 35 U.S.C. 112, first paragraph have been withdrawn.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,218,368B1	WIROSTKO	4-2001
5,190,918	DEUTCH et al.	3-1993
6,482,801B2	WU	11-2002
5,654,312	ANDRULIS, JR. et al.	8-1997
5,776,898	TEICHER et al.	7-1998
WO 95/18606	AGGARWAL	7-1995
5,952,372	MCDANIEL	9-1999

Arbiser et al. "The antiangiogenic agents TNP-470 and 2-methoxyestradiol inhibit the growth of angiosarcoma in mice". J. Am. Acad. Dermatol, 1999, June; 40 (6t 1):925-9.

Thaloor et al. "Inhibition of Angiogenic Differentiation of Human Umbilical Vein Endothelial Cells by Curcumin". Cell Growth & Differentiation, Vol. 9, pages 305-312, April 1998.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 4-6 and 17 are rejected under 35 U.S.C. 112 second paragraph as being indefinite.

Claim 17 is rejected under 35 U.S.C. 102(e) as being anticipated by Wirostko (U.S.Patent No. 6,218,368 B1).

Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deutch et al. (U.S.Patent No. 5,190,918) in view of Brem et al. (U.S.Patent No. 6,482,801B1) of record.

Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deutch et al. (U.S.Patent No. 5,190,918) in view of Andrulis Jr. et al. (U.S.Patent No. 5654312) of record.

Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deutch et al. (U.S.Patent No. 5,190,918) in view of Teicher et al. (U.S.Patent No. 5,776,898) of record.

Claims 10-12 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aggarwal (WO 95/18606) of record.

Claims 10-12 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arbiser et al. (June, 1999) of record in view of Thaloor et al. (1998) of record and further in view of Aggarwal (WO 95/18606) of record.

Claim Rejections - 35 USC § 112

Claims 4-6 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "amount effective" in claims 4 and 17 is indefinite since it is not clear what are the "effective amount" to be employed in the active agents (collagenase inhibitors, angiogenic fumagillin derivatives, 2,5-diaryltetrahydrofurans, aminophenylphosphonic acid compounds, 3-substituted oxindole derivatives, tetracyclines inhibiting collagenase or a sulfated polysaccharides) in order to inhibit angiogenesis without clear guidelines of effective amounts of the agents being utilized.

The remaining claims 5-6 are indefinite to the extent that they depend from claim 4.

Claim Rejections - 35 USC § 102

Claim 17 is rejected under 35 U.S.C. 102(e) as being anticipated by Wirostko (U.S.Patent No. 6,218,368 B1).

Wirostko teach tetracyclines are known to have "collagenase inhibition properties and used chronically as therapy for diverse diseases including acne rosacea. (column 2, lines 13-30).

Claim Rejections - 35 USC § 103

Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deutch et al. (U.S.Patent No. 5,190,918) in view of Brem et al. (U.S.Patent No. 6,482,801B1) of record.

Deutch et al. teach angiogenesis activity is defined as the ability to enhance the formation of lymph vessels (lymphangiogenesis). (column 3, lines 20-25).

Deutch et al. do not teach the collagenase inhibitors for the treatment of formation of lymph vessels (lymphangiogenesis).

Brem et al. teach tetracyclines inhibiting collagenase such as minocycline is effective inhibitors of angiogenesis. (column 3, lines 43-46 and column 2, lines 60-64).

It would have been obvious to one of ordinary skill in the art to employ collagenase inhibitors including minocycline for the treatment of lymphangiogenesis because lymphangiogenesis involves angiogenesis activity of forming a blood vessels as taught by Brem et al. One would have been motivated to employ collagenase inhibitor (e.g. minocycline) with a reasonable expectation of successfully treating formation of lymph vessels (lymphangiogenesis) with a reasonable expectation of successfully treating the disease mediated by angiogenesis.

Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deutch et al. (U.S.Patent No. 5,190,918) in view of Andrulis Jr. et al. (U.S.Patent No. 5654312) of record.

Deutch et al. teach angiogenesis activity is defined as the ability to enhance the formation of lymph vessels (lymphangiogenesis). (column 3, lines 20-25).

Deutch et al. do not teach thalidomide for the treatment of formation of lymph vessels (lymphangiogenesis).

Andrulis Jr. et al. teach that thalidomides are effective angiogenesis inhibitor. (abstract, column 1, lines 47-48, lines 55-56). Andrulis Jr. et al. teach thalidomides maybe administered topically (column 4, lines 55-60, and column 6, line 18, line 43 and line 57).

It would have been obvious to one of ordinary skill in the art to employ thalidomide for the treatment of lymphangiogenesis because lymphangiogenesis is which is formation of lymph vessels is caused by angiogenesis as taught by Deutch et al. and because thalidomides are effective angiogenesis inhibitor as taught by Andrulis Jr. et al. One would have been motivated to employ thalidomide with a reasonable expectation of successfully treating a diseased mediated by angiogenesis in order to achieve effective angiogenesis inhibition of thalidomide.

Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deutch et al. (U.S.Patent No. 5,190,918) in view of Teicher et al. (U.S.Patent No. 5,776,898) of record.

Deutch et al. teach angiogenesis activity is defined as the ability to enhance the formation of lymph vessels (lymphangiogenesis). (column 3, lines 20-25).

Deutch et al. do not teach angiogenic fumagillin derivatives such as TNP-470 for the treatment of formation of lymph vessels (lymphangiogenesis).

Teicher et al. teach that TNP-470 is an antiangiogenic agent. (column 7, lines 40-41, column 17, lines 40-50).

It would have been obvious to one of ordinary skill in the art to employ angiogenic fumagillin derivatives such as TNP-470 for the treatment of lymphangiogenesis because lymphangiogenesis is caused by angiogenesis involving formation of lymph vessels and because TNP-470 is an angiogenesis inhibitor as taught by Teicher et al. One would have been motivate do employ TNP-470 with a reasonable expectation of successfully treating a disease mediated by angiogenesis (formation of lymph vessel e.g. lymphangiogenesis) in order to achieve effective angiogenesis inhibition of TNP-470 as taught by Teicher et al.

Claims 10-12 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aggarwal (WO 95/18606) of record.

Aggarwal teach method for the treatment of melanomas (malignant melanoma), basal cell carcinoma, squamous cell carcinoma, soft tissue sarcomas, comprising administration of effective dose of curcumin (mixture of demethoxycurcumin). (page 5, lies 20-32, page 6). Aggarwal teach the composition comprising curcumin can be formulated topical in ointment form. (page, 7, lines 26-28, page 8, lines 7-15). Aggarwal teach the effective dose of curcumin and curcumin analogues are administered in a dose of from about 1 microgram to about 100milligram. (page 6, lines 6-11).

Aggarwal does not expressly teach the specific formulation set forth in claim 10.

It would have been obvious to one of ordinary skill in the art to modify the composition taught by Aggarwal in topical ointment formulation with effective range of curcumin for the treatment of malignant melanoma, basal cell carcinoma, squamous cell carcinoma, soft tissue sarcomas because Aggarwal teach curcumin composition can be formulated in topical ointment formulation with effective amount about 1 microgram to about 100milligrams and because Aggarwal teach curcumin is useful for the treatment of malignant melanoma, basal cell carcinoma, squamous cell carcinoma, soft tissue sarcomas. One would have been motivated to make such a modification in order to successfully treating malignant melanoma with topical curcumin formulation taught by Aggarwal.

Claims 10-12 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arbiser et al. (June, 1999) of record in view of Thaloor et al. (1998) of record and further in view of Aggarwal (WO 95/18606) of record.

Arbiser et al. on the abstract, teach that patients with recessive dystrophic epidermolysis bullosa (RDEB) are suggested to treat with angiogenesis inhibitors. Arbiser et al. also teach that the patients with RDEB have elevated levels of basic fibroblast growth factor (bFGF) and that angiogenesis inhibitors may antagonize the effects of bFGF. Arbiser et al. teach that there are currently no other means of treatment of the disorder, which has a nigh morbidity and mortality rate.

Arbiser et al. lack curcumin and demethoxycurcumin and specific formulation set forth in claim 10.

Thaloor et al. teach that curcumin inhibits angiogenesis. (abstract).

Aggarwal teach the composition comprising curcumin can be formulated topical in ointment form. (page, 7, lines 26-28, page 8, lines 7-15). Aggarwal teach the effective dose of curcumin and curcumin analogues are administered in a dose of from about 1 microgram to about 100milligram. (page 6, lines 6-11).

It would have been obvious to one of ordinary skill in the art to employ curcumin or curcuminoids (i.e.demethoxycurcumin) for the treatment of RDEB with topical formulation of curcumin taught by Aggarwal in the angiogenesis effective amounts because Arbiser et al. suggested that angiogenesis inhibitors are effective in treatment of RDEB and because curcumin or curcuminoids possess angiogenesis inhibiting property as taught by Thaloor et al. Further, curcumin or curcuminoids can be formulated in ointment formulation with wide range of dose form about 1 microgram to about 100milligrams as taught by Aggarwal. One would have been motivated to formulate curcumin for curcuminoids in topical formulation with angiogenesis effective amounts for the treatment of RDEB in order to avoid death of a patient with RDEB with only available angiogenesis inhibition treatment taught by Arbiser et al.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

(10) Response to Argument

Appellant's argument that the term "effective amount" is common and generally acceptable term for pharmaceutical claims and is not ambiguous or indefinite, provided that a person of ordinary skill in the art could determine the specific amounts without undue experimentation, is not persuasive because there is a plethora of active agents (collagenase inhibitors, angiogenic fumagillin derivatives, 2,5-diaryltetrahydrofurans, aminophenylphosphonic acid compounds, 3-substituted oxindole derivatives, thalidomides, penicillamine and IL12) having different chemical moieties. Therefore, it would be undue experimentation to determine effective amounts for every active agent. It is noted that these active agents do not possess common moiety and differ in physical and chemical characteristics; Appellant's one range of one active agent (curcumin) disclosed in page 14, lines 28-29 of the instant specification, may not cover all the active agents. Further, one of ordinary skill in the art reading the claim could not determine its metes and bounds regarding effective amounts of all the active agents claimed, because there is no such range provided or defined for the active agents other than curcumin in the specification. Therefore, one of ordinary skill in the art could not arrive at the "effective amount" of the claimed active agents within the single amount of the single compound (i.e. curcumin) having different chemical/physical property having different moiety.

With regard to 35 U.S.C. 102(e) rejection, Appellant's argue Wirostko describes systemic administration of tetracycline to treat acne rosacea which is different than rosacea because acne rosacea is refer to acne characterized by redness which is different than rosacea and attached a printout from the National Rosacea Society. This

is not persuasive because Appellant is comparing "acne rosacea" with "acne" in the print out rather than comparing "acne rosacea" with "rosacea". It is clear from Wirostko that tetracyclines are known to have "collagenase inhibition" properties and used chronically as therapy for diverse disease including **acne rosacea, which is Appellant's claimed rosacea, originally termed acne rosacea** by extrinsic evidence of U.S.Patent No. 5952372A, column 1, lines 12-35 by McDaniel.

With regard to 35 U.S.C. 103 rejection, Appellant argues Deutch et al.'s teaching of angiogenesis activity of ability to enhance the **formation** of lymph vessels is completely contrary to any common definition of angiogenesis, which is defined in the application at page 2 of the application and in the literature as relating to the initiation and **growth** of blood vessels. This is not persuasive because Deutch teaches that angiogenesis activity is defined as the ability to enhance the formation of lymph vessels which meets encompasses the claimed disorder of angiogenesis related disorder of lymphangiogenesis. Therefore, it would have been obvious to one of ordinary skill in the art to employ collagenase inhibitors (e.g. minocycline) for the treatment of lymphangiogenesis because lymphangiogenesis involves angiogenesis activity of forming blood vessels as taught by Brem et al. There is expectation of successfully treating formation of lymph vessel (lymphangiogenesis) with collagenase inhibitor (e.g. minocycline) because minocycline inhibits angiogenesis (defined by Deutch et al. for enhancing formation of lymph vessels) as taught by Brem et al. Appellant's argue that Andrulis does not lead one to extrapolate from lymphangiogenesis to angiogenesis nor that thee would be any expectation that thalidomide referenced by Andrulis with respect

to inhibiting angiogenesis, would be effective in preventing lymphangiogenesis. This is not persuasive because Andrulis Jr. et al. teach that thalidomides are effective angiogenesis inhibitor which involves formation of lymph vessels caused by angiogenesis as taught by Deutch et al. Therefore, one would have been motivated to employ thalidomide with a reasonable expectation of successfully treating a disease mediated by angiogenesis in order to achieve effective angiogenesis inhibition involving formation of lymph vessels taught by Deutch et al. Appellant argues Teicher is no different than Andrulis or Brem and it also discloses only a compound known to inhibit angiogenesis. This is not persuasive because Teicher et al. teach that TNP-470 is an antiangiogenic agent and that angiogenesis activity as defined by Dutch et al. as the ability to enhance the formation of lymph vessels which encompasses lymphangiogenesis. Therefore it would have been obvious to one of ordinary skill in the art to employ angiogenesis inhibitor involving formation of lymph vessels for the treatment of lymphangiogenesis. Appellant argues regarding Arbiser is not prior art to this application because it is the inventor's own publication (note that it is Dr. Arbiser to whom inquires are to be directed). This is not persuasive because the Arbiser et al. reference and inventor of present Application have different inventive entity and that Appellant has not rebut prima facie case by showing reference's disclosure was derived from Appellant's own work.

With regarding issued parent Application U.S.Patent No. 6,673, 843 drawn to formulation is not obvious, nor is the use of any of the defined conditions obvious. This is not persuasive because the formulation to be utilized in instant claims differ since it is

broader. It is noted that the patented formulation is drawn to more specific "unsaturated curcuminoids". Appellants argue that there is no motivated to treat completely different disorder with the claimed formulation, or why one would have any expectation of success based on a reference using a hugely different amount of drug (1mcg to 100mg) as compared to the amount in the claimed formulation. This is not persuasive because there is teaching from Aggarwal that the effective dose of curcumin and curcumin analogues are administered in a dose from about 1 mcg to about 100mg. This effective range encompasses Appellant's claimed range. Therefore, there is expectation of success in treatment of malignant melanoma within the range taught by Aggarwal. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Conferees:

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

6/10/06

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6/10/06